general increase in dosage from half a million units of penicillin a day for 28 days to two million units a day for six weeks, as recently recommended by Christie (1949), will improve the results of penicillin treatment.

There are, however, cases in which relapse cannot be ascribed to undue resistance of the infecting streptococcus to penicillin, and it may be that the causal organisms are so protected by dense vegetative lesions that they are inaccessible to the action of penicillin. It is now accepted that in conditions where the sources of infection are accessible the chances of a recrudescence of the infection can be greatly reduced by the removal of infected and avascular tissue after infection has been brought under control by penicillin (Hudson, Meanock, McIntosh, and Selbie, 1946). It is thus possible that surgery may yet provide a solution to the problem of persistent relapses after penicillin therapy in subacute bacterial endocarditis by evolving methods for the removal of the infected vegetations and the reconstruction of damaged valves.

Summary

Streptococci of the viridans type from cases of subacute bacterial endocarditis and from normal throats and extracted teeth have been differentiated into five serological groups.

The distribution in the five serological groups of the streptococci from subacute bacterial endocarditis is similar to that of the streptococci from throats and teeth, indicating that the streptococci of subacute bacterial endocarditis are derived from the region of the mouth.

Streptococci isolated during relapses after penicillin treatment in subacute bacterial endocarditis are usually similar in their serological and biochemical characters to the streptococci isolated before treatment, indicating that relapses are generally due to a recrudescence of the original infection and not to reinfection by another streptococcus.

The relationships of "streptococcus s.b.e." and *Str. salivarius*, as described by Sherman and his co-workers, to other members of the viridans group of streptococci are discussed.

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TREATMENT OF EARLY SYPHILIS WITH PENICILLIN COMBINED WITH NEOARSPHENAMINE AND BISMUTH

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Since the introduction of penicillin for the treatment of syphilis routine standard courses of treatment have been in use in the Army for the treatment of early cases. In 1944 the first scheme of treatment to be used consisted of 2,400,000 units of penicillin in aqueous solution given intramuscularly in 60 divided doses, each of 40,000 units. In 1946 it became obvious from a scrutiny of the records of patients so treated that there was a failure rate of 8% in the first six months (Marshall, 1946).

In consequence, a course which consisted of 4,000,000 units of penicillin in aqueous solution given intramuscularly in divided doses over a period of 12½ days was introduced at certain military hospitals. Also, in view of the fact that Eagle and his co-workers (1946) showed that there was a synergistic action between penicillin and arsenic in the treatment of rabbit syphilis, a standard scheme was introduced at certain other scheduled hospitals in the United Kingdom, consisting of 2,400,000 units of penicillin together with ten daily injections of 0.06 g. of "mapharside." In addition, at one military hospital in the United Kingdom a series of cases of early syphilis was treated by means of a somewhat similar course with the addition of 1 g. of bismuth (Willcox, 1946).

The cumulative relapse rates following treatment by means of the above four schedules were calculated by James, Mackay, and Wright (1948) in a series of 281 cases, using a formula evolved by the Honorary Consultant in Statistics to the Army. By this means it was found that the cumulative relapse rates at twelve months in the case of patients treated with 2,400,000 units of penicillin were 14% for sero-negative primary syphilis, 13% for sero-positive primary syphilis, and 17.5% for secondary syphilis. The results of the other courses of treatment were essentially much the same.

In 1946 reports from the United States had shown that penicillin K was less effective than penicillin G in the treatment of rabbit syphilis, and that commercial penicillin had tended to contain increasing amounts of penicillin K. The Subcommittee on Venereology of the Army Medical and Personnel Research Panel therefore adopted a scheme of treatment by which a total of 4,000,000 units of penicillin was given over a period of ten days, combined with a course of neoarsphenamine and bismuth (Eames, 1948); the addition of the latter conformed to the original suggestion of Harrison (1945). This schedule is the one considered here.

Treatment, Surveillance, and Sources of Material

The treatment was carried out as follows. During an initial period in hospital a course of 4,000,000 units of commercial penicillin (50,000 units in aqueous solution intramuscularly at three-hourly intervals over a period of ten days) was given. On the second, fifth, and ninth days

the patient received an intravenous injection of neoarsphenamine, 0.3 g., 0.45 g., and 0.6 g., respectively, together with an intramuscular injection of 0.2 g. of bismuth (1 ml. injectio bismuthi B.P.). On completion of this treatment, and subject to the clinical condition, the patient was returned to full military duty. Out-patient treatment was started seven days after his last injection of arsenic as an in-patient, and consisted of eight weekly injections of 0.6 g. of neoarsphenamine and 0.2 g. of bismuth. Thus the total treatment was 4,000,000 units of penicillin, together with 6.15 g. of neoarsphenamine and 2.2 g. of bismuth.

It is the routine in the Army for all cases of syphilis, after completion of active treatment, to have clinical and serological examinations at two-monthly intervals for six months, quarterly for one year, and six-monthly for a further year. A complete cerebrospinal fluid examination is carried out at the end of the first six months and also during the last six months of this surveillance. Both Wassermann and Kahn tests (qualitative and quantitative) were invariably made at each serological examination in our series of cases.

Nominal rolls of all cases treated at the special treatment centres in the United Kingdom by the schedule described above had been maintained from its inception. Thus it was possible to trace the records of all patients in whom treatment was initiated during the period December, 1946, to March, 1948, by examination of the record cards maintained at the Central Syphilis Register.

Some of the cases on the nominal rolls described above were not suitable for the purposes of this investigation, as those previously treated and cases of congenital, latent, and tertiary syphilis had been included. These were discarded, together with any case in which there was a doubt about the initial classification of the disease. All of the patients were males of military age, the vast majority falling between the ages of 19 and 25. All were suffering from early syphilis—namely, sero-negative primary syphilis, sero-positive primary syphilis, and early secondary syphilis.

In all cases of sero-negative primary syphilis the *Treponema pallidum* had been demonstrated in a scraping taken from the primary lesion and examined by dark-field. All other cases showed a positive serology, and the secondary cases showed such manifestations as a rash and/or mucous patches or condylomata. *Tr. pallidum* was demonstrated in 87% of sero-positive primary cases and in 65% of secondary cases.

The record cards of 1,284 patients were examined, and of these, after discarding those of the patients described above, 1,028 were found to conform to the terms of reference of the survey. The distribution of patients according to the stage of the disease is shown in Table I.

TABLE I.—Analysis of Cases According to Stage of Disease

Sero-negative primary	..	..	..	..	353 (34.6%)
Sero-positive primary	..	..	..	..	443 (42.9%)
Early secondary	..	..	..	..	232 (22.5%)
Total	..	..	..	..	1,028 (100%)

As the form of treatment under survey was not begun until December, 1946, it was possible to consider a maximum follow-up of only 18 months.

Criteria of Efficacious Treatment

In reviewing the results of treatment a patient was considered to have made satisfactory progress, to have relapsed, to have failed to respond to treatment, or to have become reinfected.

A case was regarded as having progressed satisfactorily if it conformed to the following criteria: (i) all lesions of syphilis had healed at the conclusion of treatment and surveillance; (ii) serological tests for syphilis were negative at the end of surveillance; and (iii) the cerebrospinal fluid examination was normal.

Relapse was diagnosed from the presence of fresh clinical manifestations of syphilis from which the *Tr. pallidum* could be isolated, or a change in serology from negative to positive, or abnormal C.S.F. findings. All patients still having a positive serology four months after treatment had ceased were classified as treatment failures, when further treatment was begun.

Patients were classified as "defaulters" at that time when for any reason they ceased to be followed up, or, alternatively, in the case of patients treated during the last months of this investigation, at the stage in which, though satisfactory progress was being made, the survey period closed. Thus a patient completing treatment in December, 1947, would be shown as "defaulting" at nine months if satisfactory progress was made up to September, 1948, as no records would be available after that date (see Table II).

TABLE II.—Showing "Default" from Surveillance

	Sero-neg. Primary	Sero-pos. Primary	Secondary	Total
Initial no. of cases examined	353	439	230	1,022
Cases completing all treatment	274	321	159	754
Cases "defaulting" in first 2 months	90	137	70	297
Cases left at beginning of 3rd month	184	183	89	456
"Defaulters" (3-5 months)	37	30	10	77
Cases left at beginning of 5th month	145	152	69	366
"Defaulters" (5-7 months)	29	32	14	75
Cases left at beginning of 7th month	113	113	54	280
"Defaulters" (7-10 months)	37	38	24	99
Cases left at beginning of 10th month	72	69	29	170
"Defaulters" (10-13 months)	34	30	15	79
Cases left at beginning of 13th month	36	38	14	88
"Defaulters" (13-16 months)	22	22	7	51
Cases left at beginning of 16th month	11	13	7	31
"Defaulters" (16-19 months)	5	9	5	19
Cases left at beginning of 19th month	6	3	1	10
"Defaulters"	6	3	1	10

The totals shown as remaining at the beginning of any one month are those making satisfactory progress only.

It is impossible to classify any case defaulting from surveillance before the fourth month of follow-up if the serology remains positive with no clinical signs of relapse. Such were therefore rejected from the pool of data. Thus, of 1,028 patients initially considered only 1,022 could be utilized, as two (0.86%) in the group diagnosed as secondary syphilis and four (0.9%) from the sero-positive primary group had to be rejected.

Results of Therapy and Discussion

Tables II, III, and IV show in crude figures the results of treatment and follow-up of all categories of patients

TABLE III.—Muco-cutaneous Infectious Relapses—Crude Figures

Months After Treatment	Sero-neg. Primary	Sero-pos. Primary	Secondary	Total
0-2	1	1	0	2
2-4	3	2	0	5
4-6	2	4 (1)	0	6 (1)
6-9	1	0	0	1
9-12	3 (2)	1	0	4 (2)
12-15	0	1 (1)	0	1 (1)
15-18	0	0	0	0
Total	10	9	0	19

Figures in parentheses denote cases considered to be possible reinfections—e.g., 2 of the 3 at 12 months.

treated. It will be seen that there is an extremely high rate of "default." This was consequent upon the rapid rate of release from the Forces over the period during which this investigation was carried out.

TABLE IV.—Total Relapses—Crude Figures

Months After Treatment	Sero-neg. Primary	Sero-pos. Primary	Secondary	Total
0-2	2	2	1	5
2-4	3	3	1	7
4-6	4	6 (1)	1	11 (1)
6-9	2	1	0	3
9-12	3 (2)	3	0	6 (2)
12-15	0	1 (1)	1	2 (1)
15-18	0	0	0	0
Total	14	16	4	34

Figures in parentheses denote cases considered to be possible reinfections—e.g., 2 of the 3 at 12 months.

Of the 353 sero-negative primary cases beginning treatment, 14 were considered to have shown unsatisfactory progress: these are analysed in detail in Table V. It will

TABLE V.—Analysis of Relapses Occurring in Sero-negative Primary Syphilis

Type of Relapse	No. of Cases					Total Cases
	2 mths	4 mths	6 mths	9 mths	12 mths	
Muco-cutaneous relapse ..		1	1	1		3
Clinically diagnosed as re-infection	1	2	1		2	6
Serological relapse	1		1	1	1	4
Asymptomatic neuro-relapse ..			1			1

be seen that no patient relapsed after the twelfth month, but, in view of the relatively small number of cases remaining (36) at the time, this is not necessarily significant. The one case of asymptomatic neuro-relapse which occurred was diagnosed on an abnormal cerebrospinal fluid found on routine lumbar puncture during the sixth month.

Of the above 14 cases considered to have relapsed six were diagnosed by the clinician concerned as reinfections. In view of the uncertainty of differentiating between relapse and reinfection at the present time, and as the cases did not completely satisfy the criteria of Halley and Wassermann (1928) or Moore (1943), they have been classified as relapses (see Table V). All these cases had been previously sero-negative, in all of them *Tr. pallidum* had been demonstrated in the new lesion, and all gave a history of recent exposure. In only two cases, both occurring one year after treatment ceased, were all Moore's criteria fulfilled (see Table VI),

TABLE VI.—Application of Moore's Criteria of Reinfection to Cases so Diagnosed Clinically

Type of Case	Serology Before Possible Reinf.	Time Since Treatment Ceased	History of Recent Exposures	New Site for Primary Sore	Change in Serology	Conclusion
Sero-neg. P.	Neg.	2 mths	Yes	No	No	M/C relapse
" " "	"	4 "	"	"	"	" "
" " "	"	4 "	"	Yes	"	" "
" " "	"	6 "	"	"	"	" "
" " "	"	1 year	"	"	Yes	Poss. reinf.
" " "	"	1 "	"	"	"	" "
Sero-pos. P.	"	6 mths	"	"	"	" "
" " "	"	6 "	"	"	No	M/C relapse
" " "	"	1 year	"	"	Yes	" "
" " "	"	15 mths	"	Yes	"	Poss. reinf.

but in neither of these was there adequate proof that the new sore occurred in a different lymphatic shed from the original. In these two cases there was a sero-reversal after the appearance of the new sore, and they can therefore be considered to be possible reinfections. In no case, however, was there any record of an infected consort being traced.

Among the 439 cases of sero-positive primary syphilis there were 20 which made unsatisfactory progress. These are analysed in Table VII, from which it will be seen that serological relapse is more common than in sero-negative primary syphilis, and that, for the first time, treatment

TABLE VII.—Analysis of Relapses and Failures Occurring in Sero-positive Primary Syphilis

Type of Relapse	No. of Cases						Total Cases
	2 mths	4 mths	6 mths	9 mths	12 mths	15 mths	
Muco-cutaneous	1	1	1				3
Muco-cutaneous and serological		1	1				2
Clinically diagnosed as re-infection			2		1	1	4
Non-infectious relapse: ..							
Serological relapse	1	1	2	1	2		7
Treatment failures:							
Serological fast	4						4

failures (serological-fast cases) appear. Those cases which were in the first instance clinically diagnosed as reinfections are considered in Table VI. Two of these cases fulfil all of Moore's criteria; but again, with the notes available, difficulty arises regarding the exact site of the alleged fresh primary sore.

Thirteen of the patients treated for secondary syphilis failed to show satisfactory progress, nine of these being treatment failures (Table VIII). There were no muco-

TABLE VIII.—Analysis of Relapses and Failures in Early Secondary Syphilis

Type of Relapse	No. of Cases						Total Cases
	2 mths	4 mths	6 mths	9 mths	12 mths	15 mths	
Serological relapse	1	1					2
Asymptomatic neuro-relapse ..			1			1	2
Treatment failures	9						9

cutaneous relapses in this group of cases, and no case was diagnosed as a reinfection.

Moore (1948) expressed the opinion, which he said was instigated by the statisticians, that in order to avoid getting a false statistical picture it would be unwise, owing to inevitable attrition, to draw conclusions about the effects of treatment in early syphilis without at least a thousand cases to begin with, and that when evaluating such material it was essential to use an actuarial method.

Of the 1,022 cases originally considered suitable, 754 completed the full scheme of treatment, and it is from this number that the cumulative relapse rates are calculated (see Table II). The results can therefore be considered as only approximate. It is impossible to assess the sampling error in the method of calculation used, and towards the latter end of the survey this is not inconsiderable.

An extremely large number of patients were lost to observation during the post-treatment surveillance period owing to release from the Service. In order to allow for this, the cumulative relapse rate (both total and infectious muco-cutaneous) has been calculated from the crude figures shown in Tables II, III, and IV. Treatment failures are not included in the cumulative relapse rates shown, but are considered separately. The method of calculation used by James, Mackay, and Wright (1948) has been utilized.

The total and infectious (muco-cutaneous) cumulative relapse rates are shown in Table IX. Here all those cases diagnosed as reinfections by the clinician concerned are classed as relapses. If the four cases which were possible reinfections (see above) are considered to be in fact such, then the rate is as shown by the figures in parentheses. It will be seen that the total cumulative relapse rate at 18 months is somewhat less for early secondary than for sero-positive primary syphilis. This is a trend which is in accordance with the results of others. For all types of

TABLE IX.—Analysis of Cumulative Rate of Relapse During Surveillance

Time	Sero-neg. Primary	Sero-pos. Primary	Secondary	Total
6 months	<i>Infectious (Muco-cutaneous) Relapse Rates</i>			
12 "	3.8% (3.8%)	4.5% (3.8%)	0%	3.3% (3.0%)
18 "	10.0% (6.6%)	6.3% (5.6%)	0%	6.6% (5.0%)
	10.0% (6.6%)	9.9% (5.6%)	0%	8.2% (5.0%)
6 "	<i>Total Relapse Rate</i>			
12 "	5.7% (9.3%)	6.9% (6.2%)	3.6%	5.7% (5.2%)
18 "	12.6% (9.3%)	13.0% (12.3%)	3.6%	12.1% (9.3%)
	12.6% (9.3%)	16.4% (12.3%)	12.4%*	15.0% (10.8%)

Figures in parentheses show cumulative relapse rates when possible reinfections are accepted as such.

* The sampling error here is considerable in view of the small number of cases involved.

cases considered the muco-cutaneous relapse rate, which from a public health point of view is an important yardstick by which to judge the efficacy of treatment, is either 8.2 or 5% at 18 months. The Clinical Co-operative Group figures (Moore, 1943) show that 85% of such relapses occur in the first two years of surveillance after long-term arsenical and bismuth therapy.

Moore (1947), utilizing a total dosage of 2,400,000 units of penicillin, quotes a cumulative relapse rate at 11 months of 15%, and of 21% for a schedule of 2,400,000 units of commercial penicillin with the addition of 320 mg. of arsenoxide (in eight daily injections each of 40 mg.). Reynolds (1948), in considering various schedules of treatment for early syphilis by means of commercial penicillin alone (totals of 4,800,000 units two-hourly for eight days, 4,800,000 units three-hourly for eight days, and 9,600,000 units three-hourly for 15 days in divided doses), gives a combined cumulative relapse rate of 16.43% during the twelfth month of follow-up. At the end of the twelfth month the cumulative relapse rate (total) for the scheme discussed in this paper is either 12.1 or 9.3%, depending, as stated above, on whether certain of the cases diagnosed as reinfections are included as relapses or not. At the end of the eighteenth month these figures are 15 or 10.8%. The cumulative relapse rates thus appear to be at least as satisfactory as, if not superior to, those obtained with the various schemes of treatment reported in the last few years.

Toxic Reactions

It was not always easy to judge from the clinical notes made at the time whether such toxic reactions as were observed were definitely due to penicillin or to arsenic. This is especially the case as regards ninth-day erythema, which tends to occur at about the same time as urticarial reactions due to penicillin. However, in most cases the clinician treating the patient expressed an opinion concerning the causation, and in cases in which there appeared to be a doubt the toxic reaction has been considered as being due to arsenic. In consequence the actual arsenical toxicity rates may in fact be less than those given below.

Reactions due to penicillin, either local or generalized, were rarely recorded. Such cases of penicillin urticaria as were noted responded to treatment, usually with no interruption of the routine antisyphilitic therapy.

There were 33 cases in which the toxic effects occurring were considered to be due to neoarsphenamine. In 28 of these no more arsenical treatment was given to the patient after the toxic reaction; in the remaining five cases treatment was interrupted, but was later resumed. Seventeen cases of arsenical toxicity occurred in the first three weeks of treatment; the remainder showed a fairly even scatter throughout the rest of the period of treatment.

Six cases of jaundice occurred in the series, but, since it is generally accepted that this condition is of infective origin, they are not included in the series of toxic effects considered to be due to neoarsphenamine. Of these six patients, one developed jaundice during the first ten days of treatment, the remaining five at intervals between two and five months after the beginning of treatment.

The following analysis of the 33 reactions caused by neoarsphenamine shows that the vast majority were in the nature of a dermatitis: *Toxico-dermal reactions*: ninth-day reaction, 9 cases; dermatitis, 19; pruritus, 1 case. *Gastro-intestinal reactions*: nausea, 1 case. *Other reactions*: encephalopathy, 1 case; agranulocytosis, 1 case; albuminuria, 1 case.

During the hospital phase of treatment, in addition to the nine cases of ninth-day erythema observed, six patients showed toxic reactions due to arsenic: of these, one developed a punctate dermatitis and treatment was interrupted for a week but was later resumed; in the five others, which included one case diagnosed as arsenical encephalopathy, treatment with neoarsphenamine was discontinued. In five of the nine cases of ninth-day erythema arsenical therapy was also discontinued. During the out-patient phase of treatment toxic reactions occurred in 18 patients, and in all of them treatment with neoarsphenamine was permanently stopped.

There was no fatality among the patients in whom toxic reactions occurred, and in only three cases could there have been considered to be a danger to life. These latter consisted of one case of exfoliative dermatitis, which occurred in a patient with sero-negative primary syphilis 74 days after the onset of treatment; one case of agranulocytosis with angina, which occurred in a patient with sero-negative primary syphilis 23 days after treatment started; and one case of arsenical encephalopathy occurring nine days after the beginning of treatment in a patient with secondary syphilis. All these patients received BAL (OX 217) in the following dosage: 4 ml. four-hourly for three doses on the first and second days of treatment, and daily doses of 4 ml. for the next two to five days.

Since records are complete for the in-patient period of treatment, toxic reactions within the first ten days can be expressed as a percentage of all cases completing hospital treatment. With regard to reactions occurring in the out-patient period of treatment (late toxic reactions), the number of patients completing all treatment and the number "defaulting" during the out-patient phase are known. A reasonable estimate of the total number exposed to the risk of toxicity will therefore be the total of those known to have completed treatment, plus half the number of patients "defaulting" during this phase (Table X). With this assumption, for all the patients

TABLE X.—Crude Figures of Number of Patients Exposed to Toxicity

	Sero-neg. Primary	Sero-pos. Primary	Secondary	Total
(a) No. of patients starting hospital treatment	353	439	230	1,022
(b) No. of patients completing O.P. treatment	274	321	159	754
(c) No. of patients completing part of O.P. treatment	79	118	71	268
(d) Estimated no. of patients exposed to risk of toxicity in O.P. portion of treatment = (b) + $\frac{1}{2}$ (c)	313	380	194	887
(e) Total no. of early toxic reactions (first-phase treatment)	5	5	4	14
(f) Total no. of early toxic reactions in which treatment stopped	3	4	2	9
(g) No. of toxic reactions in O.P. treatment phase	6	10	3	19

treated, the toxicity rate during the early portion of treatment is 1.37%, and that for the out-patient phase of treatment 2.14%—thus giving an estimated total toxicity rate of 3.51%. In Table XI these figures are broken down according to the stage of disease when first treated.

TABLE XI.—Analysis of Rates of Toxic Reactions

	Sero-neg. Primary	Sero-pos. Primary	Secondary	Total
Toxicity rate during hospital phase of treatment	1.41%	1.13%	1.72%	1.37%
Late toxicity rate	1.91%	2.63%	1.54%	2.14%
Overall toxicity rate	3.32%	3.76%	3.26%	3.51%

Summary and Conclusions

An analysis of the results of treatment of 1,028 patients treated for early syphilis, with a schedule consisting of 4,000,000 units of penicillin combined with one course of neoarsphenamine and bismuth, is described.

There was a high rate of "default" from surveillance due to the rapid release of patients from the Service. In order to offset this and to obtain a true statistical picture an actuarial method has been used.

If all patients who were considered by the clinician concerned to have become reinfected were accounted for as relapses, then the total cumulative relapse rate at 18 months was found to be 15% and the cumulative muco-cutaneous infectious relapse rate 8.2%. If four of the ten cases clinically diagnosed as reinfections are accepted as such these relapse rates would be 10.8 and 5% respectively. These results would seem to be more satisfactory than those reported by others using commercial penicillin alone and in combination with mapharside by the semi-intensive method.

Treatment failures (cases showing sero-resistance) were small in number, being 0.9% of sero-positive primary cases and 3.87% of secondary cases.

Toxic reactions were of a very low incidence, occurring in 3.51% of all patients treated, and there were no fatalities.

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The current issue of the *Practitioner* is devoted to a review of the first year's working of the National Health Service. All the contributors are anonymous, but there is an editorial assurance that they are outstanding in their own spheres. A physician concludes that "there is no evidence that the health of the nation has benefited from the first year of the National Health Service. On the other hand . . . no great harm has resulted." A surgeon puts forward a number of constructive suggestions, and an obstetrician takes the view that "the field is set for a wonderful experiment which could not fail to yield encouraging and possibly dramatic results." General practitioners put forward their own distinctive views, and two newly qualified practitioners contrast their enhanced material security with certain spiritual doubts.

SEX HORMONE UPSET IN AFRICANS

BY

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Only in the last few years has interest begun to be focused on the non-parasitic pathology of Africans. The gaps in our knowledge are so immense that it is extremely unwise to be dogmatic on any point in African pathology. Nevertheless, from the few centres where pathological investigations, and particularly necropsies, are being carried out reports are accumulating which show that there are striking differences between the incidence of various lesions in Africans and in Europeans. These have been reviewed by Lewis (1942) and Gelfand (1948). Owing to the total absence of reliable statistics it is usually very difficult to express these differences, and all figures must be interpreted with great caution. Certain of these differences are explicable on climatic or parasitic grounds, others, such as sickle-cell anaemia, on racial grounds, but the majority still defy explanation.

In this paper I suggest that certain of these so far unexplained differences are explicable on the assumption that, because of the almost universal liver damage, Africans are subject to oestrinization on almost a national scale, or even on a continental scale. As chemical analyses of the urines to ascertain sex hormone excretion have not yet been performed, it is proposed to review the evidence supporting this hypothesis.

Malnutrition in Africans

It has long been known that there is a very high incidence of liver disease in Africans and that cirrhosis is extremely common (Vint, 1931); in fact, in East Africans and in the South African Bantu it has been found to be almost universal (Davies, 1948a, b, c; Gillman and Gillman, 1948). Recently evidence has accumulated which suggests that this liver damage is largely the result of malnutrition, assisted perhaps in certain areas by the effects of parasites (Davies, 1948a, b, c). Owing to malnutrition a fatty liver develops early in childhood and cell accumulations then occur with fibrosis, with or without the deposition of iron. Cirrhosis of the liver of a Laennec type often develops even in young children. In those less affected who survive, the liver is permanently marked and often functionally upset.

After childhood is passed recurrent episodes of malnutrition or chronic infections will precipitate further attacks, so that these patients present, both clinically and pathologically, a state somewhat similar to that seen in young children. Other causes of liver damage, such as infectious hepatitis and post-arsenical jaundice, are also common in Africa, and there is reason to suppose that nutritional hepatic necrosis occurs in Africans as it is suspected to do in Ceylon (Fernando, Medonza, and Rajasuriya, 1948). Clinically, Trowell (1946) has found that this malnutritional syndrome, kwashiorkor, is extremely common in African children, and, owing to the prolonged period of breast-feeding and the absence of a proper weaning period, few African children escape without at least a minor attack of the condition. This clinical observation is fully in accord with the pathological finding of almost universal liver damage at necropsy.

There is thus evidence that from early childhood a high proportion of Africans have damaged livers. This has